Patient-centered Benefit-Risk Assessment of a Novel Therapy for Alopecia Areata

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INTRODUCTION

- Alopecia areata (AA) is an autoimmune disease, and the second most prevalent hair loss disorder after androgenetic alopecia.[1] The global AA incidence is approximately 2%.[2] Patients can experience poor health-related quality of life (HRQoL).3 Existing AA treatment options have limited success, and no cure has been found.[3]
- Ritlecitinib (PF-06651600) is an orally bioavailable, small molecule inhibitor of Janus kinase (JAK) 3 and the tyrosine kinase expressed in hepatocellular carcinoma (TEC) kinase family.[4] Recent evidence suggests that treatment with JAK inhibitors can lead to substantial hair regrowth for AA patients, versus placebo.[5] However, approved and marketed JAK inhibitors carry identified risks (such as serious infections, malignancies, thrombosis).[6]
- It is therefore important to understand patients' willingness to tolerate the identified and potential risks of treatments for conditions such as AA.

OBJECTIVE

- We aimed to understand whether ritlecitinib 50 mg once daily (QD) has a positive benefit-risk profile from the perspective of adult patients with AA.

METHODS

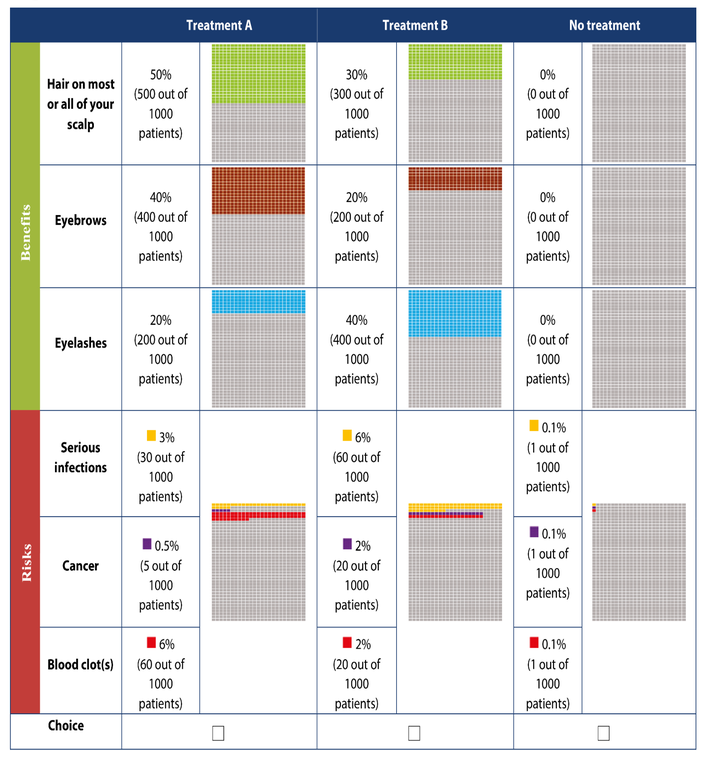
- A patient-centered benefit-risk assessment (BRA) combined preference data from a discrete choice experiment (DCE) involving patients in the United States (US) and Europe and efficacy data of ritlecitinib 50 mg daily dose and placebo from a phase IIb/III dose-ranging and pivotal clinical trial (NCT03732807).
- A DCE was used to elicit patient preferences for six attributes (**Table 1**): three benefits (chance of achieving ≥80% scalp hair regrowth, and moderate or normal eyebrow and eyelash hair) and three key risks (three-year risks of serious infections, blood clots, and cancer). In the DCE, patients were required to complete a series of choice tasks (**Figure 1**) that consisted of three alternatives: two unlabeled treatment alternatives described by combinations of attribute levels and a no-treatment option.
- This study was conducted with n=201 adult AA patients in the US, United Kingdom (UK), France, Germany, Italy, and Spain. A D-efficient design was employed to obtain a subset of all possible DCE tasks with desirable statistical properties. Preference data were modeled using an error-components logit (ECL) model. All attribute levels were coded as linear and continuous except for the levels of "Hair in eyelashes", which were coded as categorical based on specification tests.
- Clinical data were used to determine the performance of the different treatment options on the attributes included in the DCE. The attribute preference weight and treatment performance were combined to determine the value (utility) of the treatment option and attribute. These values were used to summarize the overall benefit-risk profile and probability that patients prefer one of the treatment options. Uncertainty in clinical effects were tested using stochastic multicriteria acceptability analysis (SMAA). This analysis examined the sensitivity of the net benefit-risk (NBR) scores to changes in the clinical effect estimates and preference heterogeneity for ritlecitinib 50 mg daily and placebo.

Table 1. DCE Attributes and Levels

Attribute	Description	Levels
Hair on most or all of your scalp	The chance of getting most or all of your scalp hair (80% to 100% of your scalp hair) after 24 weeks on treatment	• 0% (0 out of 1,000 patients). • 10% (100 out of 1,000 patients). • 30% (300 out of 1,000 patients). • 50% (500 out of 1,000 patients).
Eyebrows	The chance of getting moderate (mildly decreased density and/or short gaps in the eyebrows) or normal eyebrows after 24 weeks on treatment	• 0% (0 out of 1,000 patients). • 20% (200 out of 1,000 patients). • 40% (400 out of 1,000 patients).
Eyelashes	The chance of getting moderate (mildly decreased density and/or short gaps in the eyelashes) or normal eyelashes after 24 weeks on treatment	• 0% (0 out of 1,000 patients) • 20% (200 out of 1,000 patients). • 40% (400 out of 1,000 patients).
Risk of serious infections during three years of treatment	A serious infection means that you may have to stay in the hospital for treatment of the infection and/or receive treatment through an injection. The serious infection may potentially be life-threatening. You may need to temporarily (until the infection has cleared) or permanently stop your AA treatment. Examples of such infections may include lung infection, shingles, urinary tract infection, etc.	• 0.1% (one out of 1,000 patients treated for three years). • 3% (30 out of 1,000 patients treated for three years). • 6% (60 out of 1,000 patients treated for three years).
Risk of cancer during three years of treatment	Cancer typically requires chemotherapy or surgery, and some cancers can be life-threatening. Some cancers can be treated or cured with treatment, while others may not be treatable. You may need to temporarily or permanently stop your AA treatment.	• 0.1% (one out of 1,000 patients treated for three years). • 0.5% (five out of 1,000 patients treated for three years). • 2% (20 out of 1,000 patients treated for three years).
Risk of blood clots during three years of treatment	Blood clots require treatment with blood-thinning medication, may require you to stay in the hospital for treatment, and in some cases may potentially be life-threatening. You may need to temporarily or permanently stop your AA treatment.	• 0.1% (one out of 1,000 patients treated for three years). • 2% (20 out of 1,000 patients treated for three years). • 6% (60 out of 1,000 patients treated for three years).

AA = alopecia areata

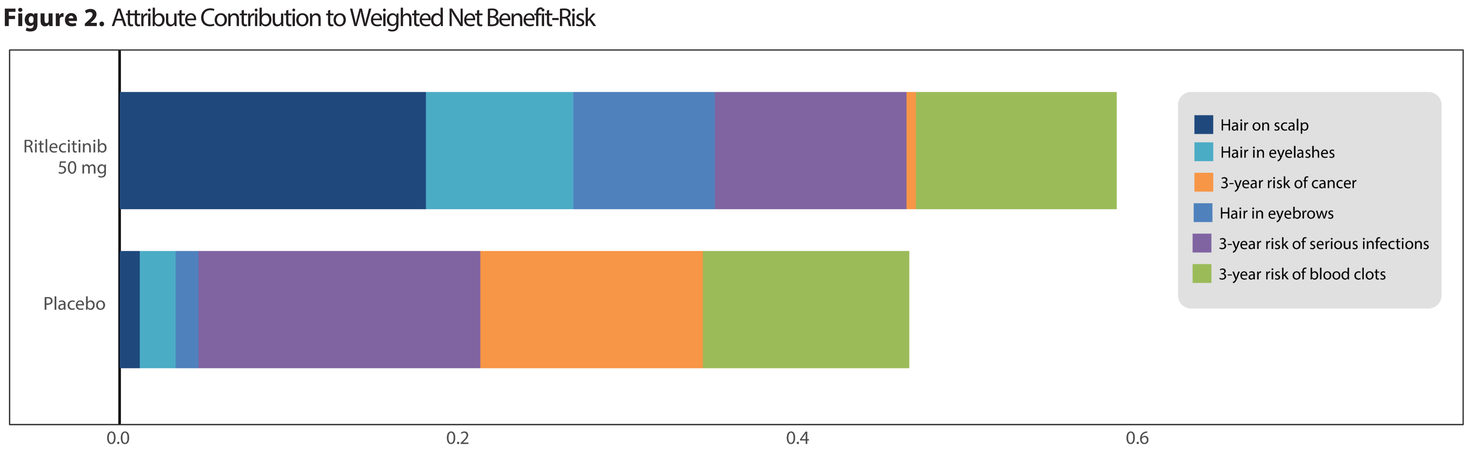
Figure 1. Example DCE Question



RESULTS

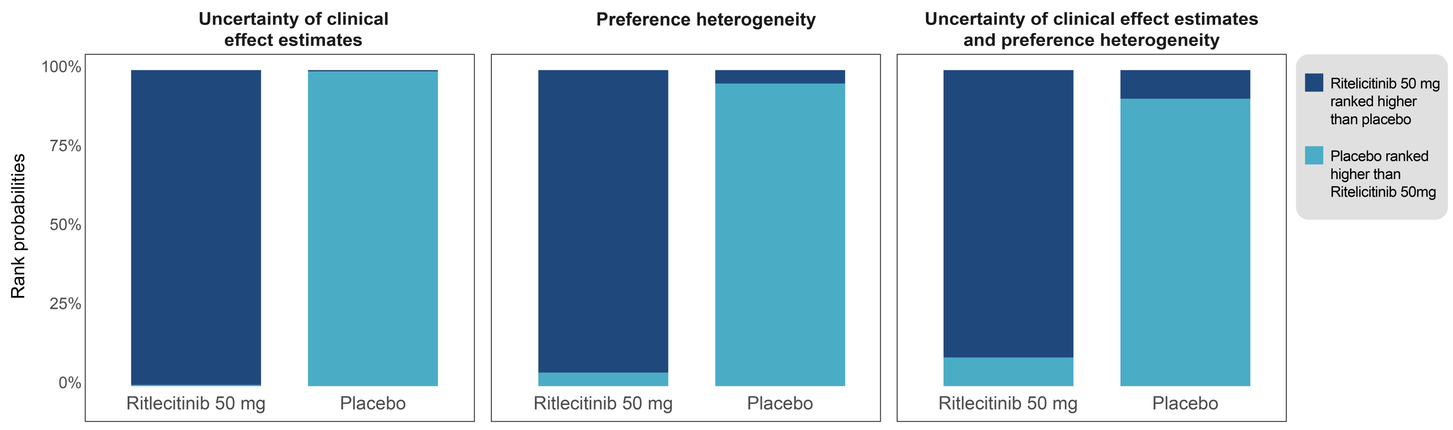
- This study demonstrated that patient preferences for AA treatments was mainly driven by the treatment success of hair regrowth on the scalp after 24 weeks of treatment. While the avoidance of treatment-related risks was important to patients, they were willing to accept a higher level of each risk in return for a higher probability of hair regrowth.

Figure 2. Attribute Contribution to Weighted Net Benefit-Risk



- Ritlecitinib 50 mg daily achieved a higher NBR score (0.587) than placebo (0.465) (**Figure 2**) and was expected to be preferred over placebo by patients with AA (predicted choice probability=65.9%; 95% confidence interval 59.4, 71.5). In sensitivity analyses, ritlecitinib had higher NBR scores than placebo, with 99.8% probability when accounting for uncertainty in the clinical effect estimates, 95.7% when accounting for preference heterogeneity, and 90.9% when accounting for both (**Figure 3**).

Figure 3. Effect of Uncertainty: Clinical Data, Preferences, and Both



- Various sensitivity analyses confirmed the robustness of the positive benefit-risk profile of ritlecitinib 50 mg. The conclusions were insensitive to changes in individual attribute weights as well as to changes in the performance estimates of individual benefit and risk endpoints of both ritlecitinib 50 mg and placebo. Further, the multi-way sensitivity analyses confirmed that ritlecitinib 50 mg would retain its positive benefit-risk profile with most plausible parameters in the BRA model, i.e., while considering simultaneous uncertainty in the clinical effect estimates due to limited clinical trial sample sizes and heterogeneity in preferences among patients with AA.

CONCLUSIONS

- Ritlecitinib 50 mg QD demonstrated a positive benefit-risk profile compared to placebo from the perspective of adult patients with AA. These findings may help to inform regulatory agencies, payers, clinicians, and patients considering ritlecitinib for the treatment of AA.

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DISCLOSURES

This study was sponsored by Pfizer, Inc. EL, BH, JM, and DM are employees of Pfizer, Inc, and hold stock or stock options in Pfizer Inc.
CW, NK, and MT are employees of Evidera.
TT was an employee of Evidera at the time of the study.
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